Eur J Vasc Endovasc Surg 25, 360–366 (2003)
doi:10.1053/ejvs.2002.1790, available online at http://www.sciencedirect.com on SCIENCE DIRECT

SHORT REPORT

# Aneurysm of an Expanded Polytetrafluoroethylene Vascular Graft: an Ultrastructural Evaluation

**N. Chakfé*[1], F. Dieval[2], F. Thaveau[1], I. Taghavi[1], J.-F. Le Magnen[2], G. Laroche[3], O. Hassani[1] G. Riepe[4], B. Durand[2] and J.-G. Kretz[1]**

*Groupe Européen de Recherche sur les Prothèses appliquées à la Chirurgie Vasculaire, Université Louis Pasteur, Strasbourg:*
*[1]Department of Cardio-Vascular Surgery, Les Hopitaux Universitaires de Strasbourg, Strasbourg, France,*
*[2]Laboratoire de Physique et Mécanique Textile, Université de Haute Alsace, Mulhouse, France,*
*[3]Institut des Biomatériaux du Québec, Québec, Canada and [4]Department of General, Thoracic and Vascular Surgery, Hamburg, Germany*

*Key Words: Blood vessel prosthesis; Polytetrafluoroethylene; Aneurysm.*

## Introduction

Long-term degradation of vascular prostheses remains a problem for vascular surgeons. The etiology of late degradation is probably multifactorial. It includes chemical degradation of the polymer as well as structural defects and may lead to dilatation or rupture of the prosthesis. Expanded polytetrafluoroethylene (ePTFE) prostheses were first experimentally[1] and clinically[2] introduced in 1972. They are now widely used as vascular substitutes of small arteries, mainly for infra-inguinal revascularizations. These prostheses have good mechanical properties which are related to the manufacturing process. Expanded PTFE is obtained by an extrusion process followed by sintering that create the specific microporous structure of nodes of high cristallinity linked together by oriented fibrils. Cases of spontaneous dilatation, leading to the rupture of the prosthesis in one case, were reported for the first generation of grafts.[3–5] No more cases of dilatation have been reported in the literature. Since the manufacturers modified the design and improved the manufacturing process.

* Please address all correspondence to: N. Chakfé, Department of Vascular Surgery, Les Hopitaux Universitaires de Strasbourg, BP No. 426, 67091, Strasbourg Cedex, France.

We report an exceptional case of an aneurysm of a ePTFE prosthesis which occurred 3 months after its implantation and discuss the underlying mechanism.

## Case Report

A 54-year-old woman was admitted with a three day history of acute right lower limb ischaemia caused by occlusion of a 7 mm diameter ePTFE above-knee femoropopliteal bypass (Carboflow®, Impra Inc, Tempe, AZ, U.S.A.). The prosthesis was implanted 3 months before for a critical limb ischaemia with painful malleolar ulcers related to an arteriosclerotic occlusion of the superficial femoral artery and of the peroneal artery (ankle systolic pressure: 70 mmHg, ankle-brachial index: 0.5).

Pre-operative angiography confirmed occlusion of the femoropopliteal bypass without distal perfusion. Surgical thrombectomy of the prosthesis was performed through a groin incision. A Fogarty catheter retrieved much thrombus with a poor back blooding. Per-operative angiography showed an aneurysm of the distal portion of the prosthesis, just above the anastomosis (Fig. 1). The distal portion of the prosthesis was surgically exposed to reveal a true aneurysm of the ePTFE graft (Fig. 2). This portion was resected and the continuity of the prosthesis

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**Fig. 1.** Per-operative view of the ePTFE aneurysm.

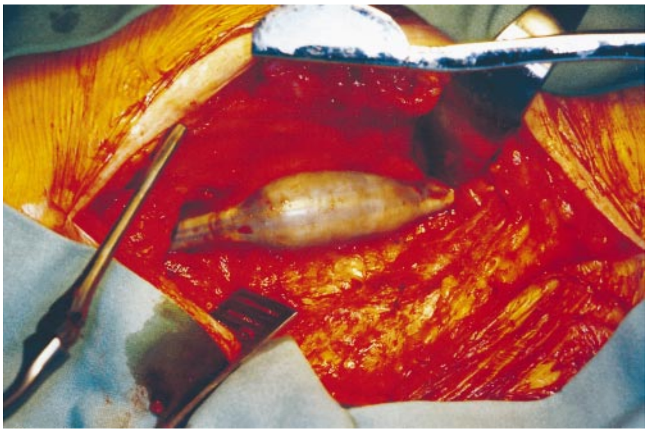

**Fig. 2.** Per-operative angiography after desobstruction demonstrating the ePTFE aneurysm.

reestablished with a new segment of ePTFE prosthesis that thrombosed on the first post-operative day.

The explanted prosthesis was cleaned in order to undertake chemical investigations. It was immersed in a 10% sodium hypochlorite solution with soft agitation for about 3 h, followed by rinsing in distillated water. Hypochlorite remnants were neutralized using a 0.5% hydrogen peroxide solution. The prosthesis was rinsed again in distillated water, dried and stored.

Macroscopic examination after washing the explanted prosthesis showed no abnormal deposits, no holes and no tears on the surface of the aneurysm. The volume corresponding to the 30 mm of the aneurysm was about 8.1 $cm^3$ and consequently 4 times higher than the 1.9 $cm^3$ volume of a straight 7 mm diameter tube. The surface of the aneurysm measured 19.73 $cm^2$ and was consequently 3 times higher than the 6.15 $cm^2$ surface of a straight 7 mm diameter tube.

## Investigations

### *Scanning electron microscopy*

Scanning electron microscopy without metallization of the specimens (Hitachi S-2360N, Elexience, Verrières le Buisson, France) was used to measure the thickness of the prosthesis on 3 different portions of the aneurysm (ND area: area of non dilated graft, MD area: area of maximum dilatation of the aneurysm, and ID area: area of intermediate dilatation of the aneurysm), and also to characterize the structure of the prosthesis with the following parameters: the mean internodal distance (MIND), the thickness, length, perimeter, and surface of the nodes, the mean interfibrils distance (MIFD), and the thickness of the fibrils using image analysis software (NIH Image 1.61, NIH Wayne Rasband, U.S.A.). We compared theses results to those taken from five virgin Impra Carboflow® prostheses taken from five different manufacturing lots. Mean thickness, length, perimeter, and surface of the nodes were calculated from measures realized on 200 nodes randomly chosen on the surface analized. The MIND and the thickness of the prosthesis was calculated from 40 measures. The MIFD and the thickness of the fibrils were calculated from 40 measures.

### *Differential scanning calorimetry*

A computer controlled differential scanning calorimeter (Metler – Toledo DSC 30, Switzerland) was used to analyze the thermal properties of ePTFE specimens taken from the three previously described areas of the explanted prostheses and on the five different virgin prostheses which were submitted to the same washing process as the explanted prostheses. The samples, weighing from 10 to 20 mg were placed in solid standard aluminum pans. The measurements were made from −150 to 400 °C in an atmosphere of nitrogen at a scanning rate of 5 °C/mn. The system was previously calibrated with Indium at 156.6 °C. (DSC sign ICTA: 1, Tau Lag: 15.70, Tau Signal: 0, E Dimin. Fact: 0.88, S: 2200.00). We determined the average melting temperature ($T_m$) and the heat of fusion ($\Delta H$) on the five virgin prostheses and on the dilated explanted prosthesis. The measurements were made on four samples of the same lot for the virgin prostheses, and on one sample of the previously described areas of the explanted prostheses.

### *Infra-red spectroscopy*

FTIR spectra were recorded using a Nicolet Magna-550 spectrometer (Nicolet, Madison, WI, U.S.A.) equipped with a deuterated triglycine sulphate (DTGS) detector and a germanium-coated potassium bromide (KBr) beamsplitter. One hundred scans were routinely acquired with an optical retardation of 0.25 cm to yield a 4 $cm^{-1}$ resolution. For surface characterization, the attenuated total reflection (ATR) mode was used to obtain the infrared spectra using a Split Pea attachment (Harrick Scientific Corp., Ossining, NY, U.S.A.) equipped with a silicon hemispherical 3 mm-diameter internal reflection element (IRE). The IRE was beveled along the edge of its flat surface to provide a sampling area slightly larger than the 150–200 μm diameter hot spot on the crystal.

## Results

### *Scanning electron microscopy*

Observations made on the explanted prosthesis demonstrated differences to the virgin prostheses (Table 1). The structure was even different on the ND area of the explanted prosthesis. The main differences were observed on the nodes. They appeared to have a different shape and were smaller than those of the virgin prostheses, with occasional presence of fissures (Fig. 3). Image analysis measurements demonstrated that the nodes had about the same thickness, but a lower length than the mean length measured on the virgin prostheses (77.14 μm vs 124.10 μm). Consequently, the perimeter and the surface of the nodes were smaller (167.5 μm vs 262.09 μm for the perimeter, and 605.28 $\mu m^2$ vs 1003.59 $\mu m^2$ for the surface). The dilatation of the prosthesis in MD and ID areas induced the following changes when compared to the observations made in ND area. The wall thickness of the ND area (461.44 μm) decreased to 313.03 μm in ID area and 253.68 μm in MD area. The MIND decreased slightly from 28.53 μm in ND area to

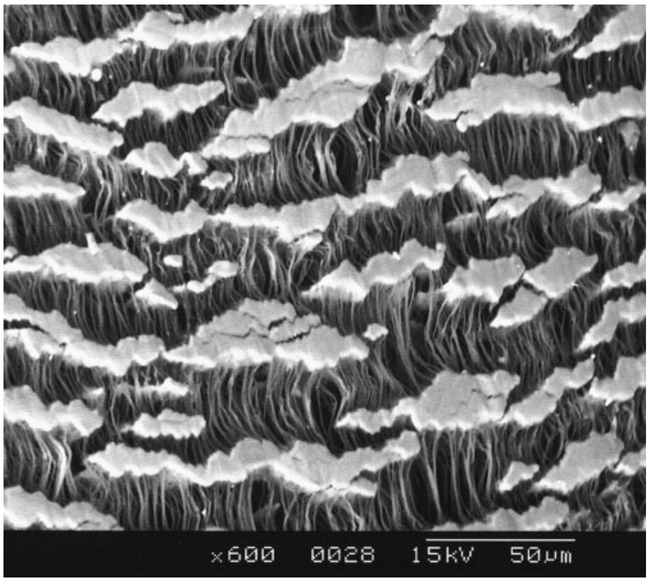


**Fig. 3.** Scanning electron microscopy of the outer surface of the explanted ePTFE Carboflo prosthesis at the level of the non-dilated area. The nodes are shorter than those of the virgin prostheses and present some fissures.

**Table 1. Comparison of the characteristics of the microporous structure of the explanted graft to the virgin ePTFE grafts (mean ± SD).**

| | Wall thickness (μm) | Internodal distance (μm) | Node thickness (μm) | Node length (μm) | Node perimeter (μm) | Node surface ($\mu m^2$) | Interfibrils distance (μm) | Fibrils thickness (μm) |
|---|---|---|---|---|---|---|---|---|
| Virgin grafts | 458.7 ± 1.916 | 29.10 ± 0.767 | 7.30 ± 0.252 | 124.21 ± 10.11 | 262.17 ± 20.67 | 1003.59 ± 75.39 | 3.03 ± 0.052 | 0.49 ± 0.009 |
| Explanted graft non dilated | 461.44 ± 23.93 | 28.53 ± 4.91 | 6.73 ± 2.26 | 77.14 ± 84.52 | 167.75 ± 171.10 | 605.28 ± 735.34 | 2.90 ± 1.10 | 0.49 ± 0.11 |
| Explanted graft maximum dilatation | 253.68 ± 7.85 | 23.63 ± 6.2 | 5.62 ± 1.71 | 349.35 ± 410.97 | 709.93 ± 824.16 | 2417.36 ± 3185.45 | 2.02 ± 1.45 | 0.32 ± 0.11 |
| Explanted graft intermediate dilatation | 313.03 ± 23.86 | 24.30 ± 5.78 | 5.12 ± 1.68 | 276.80 ± 332.02 | 561.00 ± 666.73 | 1726.64 ± 2308.69 | 2.49 ± 1.22 | 0.43 ± 0.16 |

24.30 μm in ID area and 23.63 μm in MD area. Alterations on the fibrils consisted in a slight decrease of the MIFD, and of the fibril thickness in dilated areas with a disorganization of their structure (Fig. 4). These fibrils were different when compared with those of the virgin prostheses where they were constituted by the conjunction at their contact with the nodes of few small fibrils creating one straight fibril. On the other hand, fibrils of the dilated prostheses were dissociated and thinner than those of the virgin prostheses.

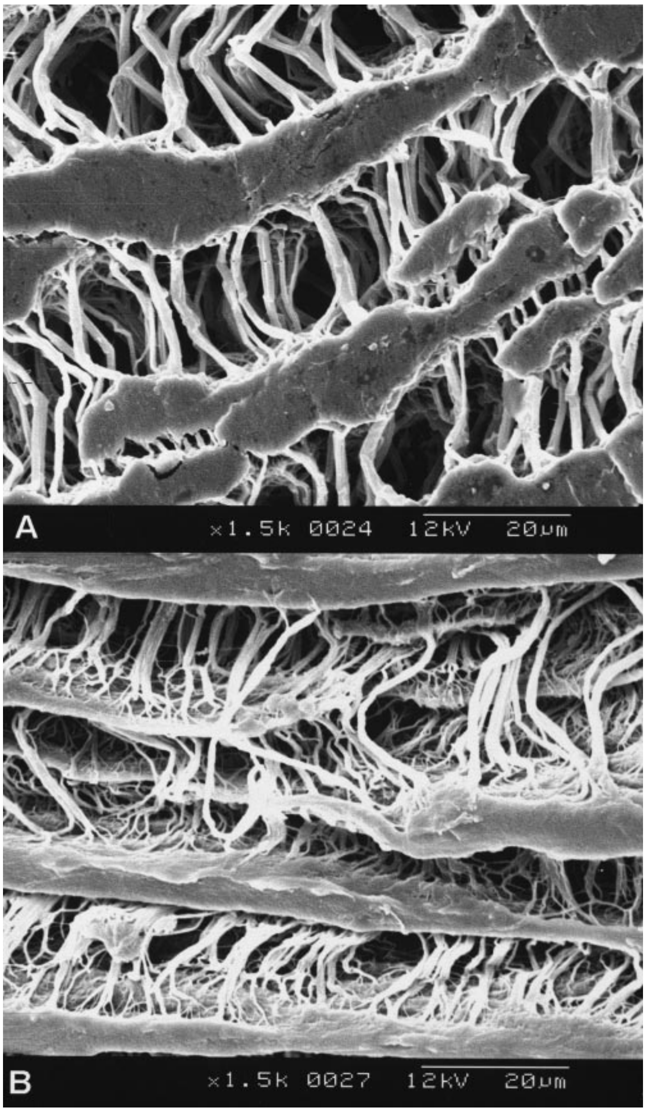


**Fig. 4.** Scanning electron microscopy of the outer surface of a virgin prosthesis (A): The fibrils are constituted by the conjunction at their contact with the nodes of few small fibrils creating one straight fibril. On the outer surface of the dilated explanted ePTFE Carboflo prosthesis, fibrils were dissociated and thinner than those of the virgin prostheses.

*Differential scanning calorimetry*

Differential scanning calorimetry performed on the virgin prostheses showed two endothermic peaks in the range of temperature studied. There was a small endothermic peak at 20 °C and a major fusion peak centered at 328 °C. The analyses of the virgin prostheses did not showed any differences between the five different lots on the first peak. However, the analysis of the second peak showed slight differences, depending of the lot.

The DSC thermogram of the ePTFE coming from the dilated region of the explanted prosthesis revealed a lower ΔH associated with the low temperature endotherm, in comparison to a virgin specimen or the non-dilated region of the explanted graft (Table 2) (Fig. 5). The amount of explanted material was not sufficient to perform enough experiments to allow statistical analysis. The second peak at 328 °C did not show significant differences between the virgin and the dilated prostheses. A very minor modification of the level of the ePTFE crystallinity may be assumed,

**Table 2. Differential Scanning Calorimetry of the explanted dilated prosthesis and of the virgin ePTFE Carboflo® prostheses ($T_m$: average melting temperature, ΔH: heat of fusion).**

| | First peak | | Second peak | |
|---|---|---|---|---|
| | ΔH (J/g) | $T_m$ (°C) | ΔH (J/g) | $T_m$ (°C) |
| Virgin ePTFE | 6.1 | 20.1 | 32.4 | 328.0 |
| Explanted prosthesis non dilated | 6.5 | 20.2 | 34.3 | 328.8 |
| Explanted prosthesis major dilation | 4.9 | 18.3 | 31.9 | 330.1 |
| Explanted prosthesis intermediate dilation | 5.0 | 19.0 | 30.5 | 330.2 |

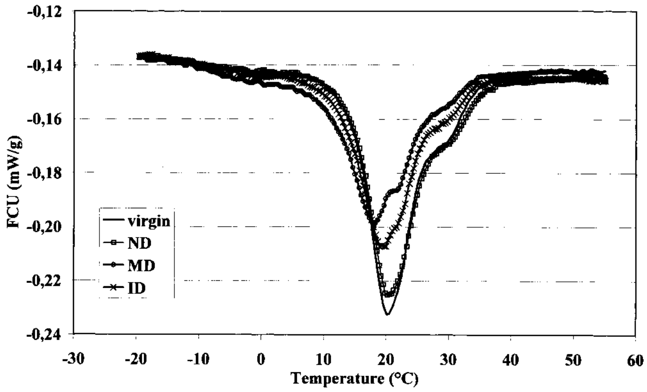


**Fig. 5.** Differential Scanning Calorimetry analysis of the explanted prosthesis and of virgin prostheses. The curve is focused on the first peak at 20 °C.

but is probably not the origin of the prosthesis deformation.

### *Infra-red spectroscopy*

Figure 6A displays the infrared spectrum of a ePTFE virgin prosthesis. Due to the simple chemical structure of PTFE (-$CF_2$−)$_n$, the infrared spectrum of this polymer only shows few features. Basically, the peaks observed 1200 and 1150 $cm^{-1}$ are assigned to asymmetric and symmetric stretching mode vibrations of the -$CFCF_2$− moieties, respectively, while the lower frequency features are due to various deformation modes of these same moieties. The infrared spectrum of the dilated region of the explanted prosthesis displays additional features (Fig. 6B). Some of these peaks are due to the presence of lipids that infiltrate the prosthesis wall through a process referred to as pseudo-atherosclerosis.[6] However, two additional spectral components neither belonging to PTFE nor lipids are clearly observed at 1580 and 1540 $cm^{-1}$. Despite extensive search in FTIR spectral libraries, no clear assignments may be provided. It is the first time that we have observed such peaks in the infrared spectra of explanted ePTFE vascular prostheses, having already analyzed more than 500 of these specimens through this analytical technique.[6]

## Discussion

Expanded polytetrafluoroethylene prostheses were first experimentally[1] and clinically[2] introduced in 1972. In 1976, Campbell *et al*. reported the encouraging results of the first clinical study of the implantation of this new kind of prosthesis on 15 patients for limb salvage.[7] However, despite high patency rates, further clinical studies reported cases of aneurysmal dilatations, one of this dilatation leading to the rupture of the prostheses.[3–5] The two main manufacturers addressed this problem in two ways. W.L. Gore and Associates applied a thin wrapping film of ePTFE on the outer surface of the graft in order to improve their strength and avoid excessive tissue proliferation.[8] Impra added radial strength to the graft to ensure a better biostability and resistance to dilatation with pulsed blood flow.[5] Since these modifications, dilatation became rare because of the good mechanical properties and the high biostability of the grafts after implantation.[9] The reasons for these dilatations have not been completely understood. Campbell *et al*.[3] suggested that two factors predisposing the occurrence of dilatation: a high arterial pressure and the use of tapered prostheses. They found that tapered prostheses had a thinner wall at their large diameter extremity than at their small extremity because of their manufacturing process.

This case of spontaneous aneurysm of an ePTFE prosthesis is to our knowledge the only published case in the literature since the 70's. Scanning electron microscopy analysis demonstrated that the non-dilated area of the explanted prosthesis showed no significant differences of wall thickness and mean internodal distance compared with the virgin prostheses. However, the nodes were shorter and consequently had a shorter perimeter and surface. They also demonstrated some fissures. The analysis of the aneurysmal part of the prosthesis showed that dilatation led to a decrease of the wall thickness and of the mean internodal distance. The dilatation created a huge modification of morphology of the nodes. The nodes thickness decreased since their length increased leading to a 2.5 times increased perimeter and surface of the nodes. The elongated nodes also demonstrated longitudinal splits that could be the consequence of the fissures observed on the non-dilated nodes. A dissociation of the fibrils at the contact of the nodes was also observed. Our observations were consistent with those of Salzmann *et al*.[10] who studied the effects of balloon dilatation on the ePTFE structural characteristics. They demonstrated that the ePTFE structure was altered by the dilatation.

The differential scanning calorimetry analyses of the explanted prosthesis demonstrated no significant modifications of the crystalline structure of the polymer. The second fusion peak at 328 °C of the different areas of the explanted and virgin prostheses were similar. According to McClurcken *et al*.[11] there was no significant proportion of unsintered ePTFE in the explanted prosthesis.

The infrared spectra of the explanted prosthesis revealed the presence of spectral features, at 1580 and 1540 $cm^{-1}$, that may not be assigned to vibrational modes of ePTFE. Even though the origin of these new features can not be determined with certainty, some hypotheses may be raised to take into account for their presence. Firstly, the presence of these additional infrared peaks may be due to the adsorption of biological molecules that would have occurred during the residence of the prosthesis in the patient's body. This is most unlikely as we never observed such features in the infrared spectra of more than 500 explanted prostheses.[6] Secondly, the appearance of new bands has also been reported when a polymer degradation occurred.[12] Again, this seems unlikely as PTFE is known to be one of the most stable polymer towards chemical degradation. Finally, one may suspect the presence of residual additives that, for

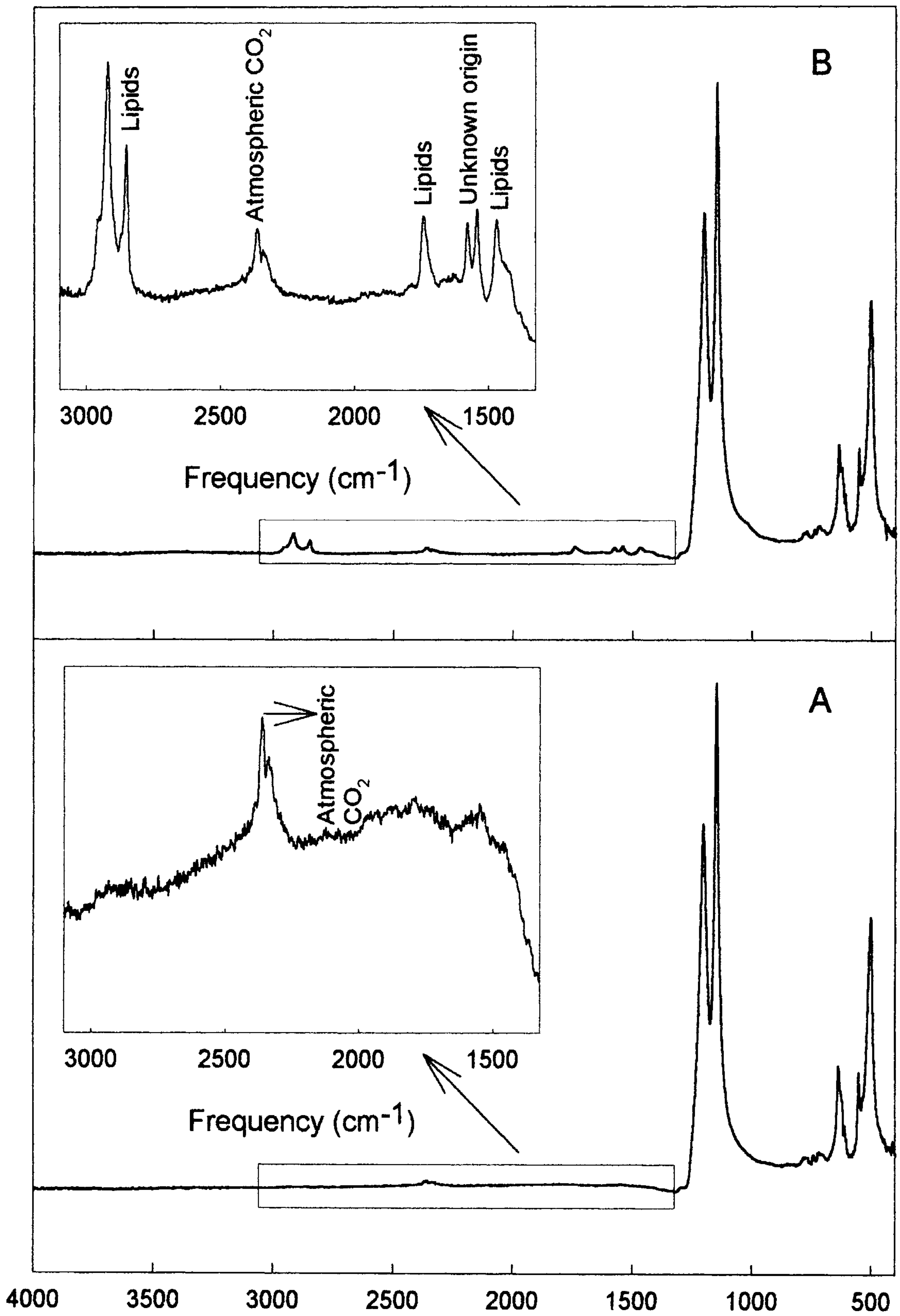


**Fig. 6.** Fourier transform infrared spectra of a ePTFE virgin prosthesis (A) and of the explanted prosthesis (B). The inserts show an enlarge view of the spectral region where additional features are observed for the explanted prosthesis.

unknown reasons, would not have been remove during the processing of this particular prosthesis. The origin of such an additive remains unclear.

ePTFE has a strong affinity with lipids[6] that may induce plastic deformation of the prosthesis.[13] Nevertheless, the amount of lipid found onto the surface of the explanted prosthesis was not higher than that observed for other explanted prostheses.[6] A better knowledge of the behavior of ePTFE prostheses may help us to understand such rare complications better. It will also help to predict the long term behavior of ePTFE grafts which are balloon-dilated for endovascular surgery procedures[14,15] or for the construction of distal anastomotic cuffs. Dilatation of ePTFE prostheses induces alterations in of the structure may modify the healing characteristics of the prosthesis.[16,17]

In conclusion, spontaneous aneurysmal dilatation of a ePTFE prosthesis is exceptional. The chemical and morphological analysis of the ePTFE structure of the explanted prosthesis did not allow us to determine the mechanism of this spontaneous dilatation. Further studies will be necessary to understand not only spontaneous dilatation but also the effect of balloon dilatation on the long term behavior of ePTFE grafts.

*Acknowledgments*

Our works on the degenerative complications of vascular prostheses have been supported by the Lucien Dreyfuss Fundation, the Regional Council of Alsace, the "Comité Ad Hoc de Surveillance des Prothèses Vasculaires" of the French Society for Vascular Surgery and the Entente Franco Allemande Fundation.

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*Accepted 23 September 2002*